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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

NOTIFICATION DATE	DELIVERY MODE
05/21/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/540,392	MARKUS, BEIER	
	Examiner	Art Unit	
	TERESA WESSENDORF	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-38* is/are pending in the application.

4a) Of the above claim(s) *20-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,19 and 22-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 18-38 are pending.

Claims 20 and 21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention and species.

Claims 18-19 and 22-38 are under examination. (Please note that claim 24 erroneously depends on cancelled claim 1. It is presumed that applicants are referring to claim 18 and the examiner presumed such.)

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102

Claims 18-19, 24-25, 27-28, 30-34 and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Schuetz et al (Journal of Analytical Chemistry (1999), 363(7), 625-631) for reasons of record as reiterated below.

Schuetz et al discloses throughout the article at e.g., the abstract:

> A multianalyte immunosensor array can he implemented by immobilization of different haptens in distinct areas of a single cavity or flow cell. In this case a mixture of different antibodies for different analytes is used in an indirect ELISA-format. The selection of the right hapten structures is very important to build up an array successfully. A system of independent hapten/antibody

combinations is needed, with one immobilized hapten (coating antigen) reacting only with one antibody. If more than one antibody binds to a coating antigen no ideal calibration curves are obtained. This phenomenon is known as shared-reactivity and can lead to double-sigmoidal curves. To use monoclonal antibodies to 2,4,6 trinitrotoluene (TNT) and 2,4-dichlorophenoxyacetic acid (2,4-D), two different haptens had to be found, one only reacting with the TNT-antibody, the other only binding to the 2,4-D-antibody. 2,4-Dichlorophenoxybutyric acid was used for the 2,4-D antibody and 2,4,6-trinitrophenyl-8-aminooctanoic acid for the TNT antibody. Although 4-nitrotoluene, 2,4-dinitrotoluene and 4-amino-2,6-dinitro-toluene showed only very low cross reactivities to the 2,4-D antibody, the corresponding haptens 4-nitrophenyl-acetic acid, 2,4- dinitrophenyl-6-aminohexanonic acid, and 4-amino-2,6-dinitrotoluyl- (N)-glutarate are useful coating antigen for this antibody….. It could he shown that the affinity consts. of an antibody to the analytes are the main sensitivity and selectivity determining parameters for competitive immunoassays. A two-dimensional microtiter plate array was used to determine the analytes 2,4-D and TNT in parallel with a mixture of antibodies.

See further the specifics of the method at e.g., page 626 under the Materials and methods section.

Accordingly, the method of Schuetz which uses specific process steps using the specific haptens and polymeric receptors fully meet the broad claimed method utilizing broad components therein.

Response to Arguments

Applicant points out that Schuetz discloses a multianalyte immunosensor array using specific haptens which are immobilized in different areas on a solid surface. While the solid surface can be a single cavity or flow cell, in the examples, Schuetz immobilizes the specific hapten derivatives on 96-well microtiter plates to determine the analytes. Schuetz uses the hapten group as a receptor. In contrast to this, in the present invention the hapten groups are different from the receptors. The receptors may be synthesized on the haptens but the haptens themselves are not the receptors. This is clear from the fact that the receptors in the present invention are synthesized in predetermined zones on the carrier not just immobilized on the carrier. Thus, Schuetz does not disclose a method for synthesizing receptors in predetermined zones on a carrier or passing liquid with receptor building blocks over predetermined zones on the carrier so that the receptors are synthesized in situ from individual receptor building blocks. In addition, Schuetz does not use a microfluidic carrier as recited in the present claims.

In reply, the claims do not recite for distinguishing features to differentiate a receptor from a hapten. Note that Schuetz recites a species for the hapten and a species for the receptor albeit, it is also immobilized as argued. However, the recited function for hapten (claim 2, step b) is not distinguishing it from the prior art. Furthermore, except for the functional term for the hapten "for receptor synthesis" however, there is no synthesis step for the receptor in the claims. Schuetz immobilization of the receptor would indicate that it was synthesized in the carrier. Applicant's arguments with respect to microfluidic carrier are not commensurate in scope with he claims which does not recite that said carrier is microfluidic, at least for claim 18.

Claim Rejections - 35 USC § 103

Claims 18-19 and 22-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Stahler et al (WO 0013018)(I) or (WO 0289971)(II) or (WO 02/32567)(III) in view of anyone of Wu et al (7034134) or Gray et al (6555310) or Edwards (6455280) for reasons of record as repeated below.

Stahler et al (I) discloses throughout the entire document at e.g., page 2 and the claims a method for producing a carrier

for the determination of analytes, comprising: (a) providing a microfluidic carrier, (b) passing liquid with receptor building blocks for synthesizing polymeric receptors over predetermined zones on the carrier, (c) immobilizing the receptor building blocks in said predetermined zones on the carrier and (d) repeating steps (b) and (c) until the desired receptors have been synthesized in the predetermined zones using the receptor building blocks, wherein hapten groups are applied to the carrier before, during or/and after the synthesis of the receptors. (U.S. No.7, 097,974 is the national stage entry of WO 0013018, as stated in the Remarks submitted on 6/10/2008.)

See the abstract of each of the Stahler (II) and (III) references. (Please note applicants' remarks made on 6/10/2008, with regards to the corresponding US applications of these two WO Patents).

None of the Stahler references teaches a hapten attached to the carrier. However, Wu discloses throughout the patent at e.g., col. 127, lines 23-27:

> Protein fusions involving polypeptides of the present invention, including fragments and/or variants thereof, can be used for the following…….determination of protein-protein interactions via immunoprecipitation, purification of proteins via affinity chromatography, functional and/or structural characterization of protein……. also encompasses the application of hapten specific antibodies for any of the uses referenced above for epitope fusion proteins. For

example, the polypeptides…. could be chemically derivatized to attach hapten molecules (e.g., DNP,…_. Due to the availability of monoclonal antibodies specific to such haptens, the protein could be readily purified using immunoprecipation, for example.

Gray et al discloses throughout the patent at e.g., col.

13, line 10 up to col. 14, line 56:

Selection of polyvalent library members is performed by contacting the library with the receptor for the tag component of library members. Usually, the library is contacted with the receptor immobilized to a solid phase and binding of library members through their tag to the receptor is allowed to reach equilibrium. The complexed receptor and library members are then brought out of solution by addition of a solid phase to which the receptor bears affinity (e.g., an avidin-labelled solid phase can be used to immobilize biotin-labelled receptors). Alternatively, the library can be contacted with receptor in solution and the receptor subsequently immobilized. The concentration of receptor should usually be at or above the Kd of the tag/receptor during solution phase binding so that most displayed tags bind to a receptor at equilibrium. When the receptor-library members are contacted with the solid phase only the library members linked to receptor through at least two displayed tags remain bound to the solid phase following separation of the solid phase from library members in solution. Library members linked to receptor through a single tag are presumably sheared from the solid phase during separation and washing of the solid phase. After removal of unbound library members, bound library members can be dissociated from the receptor and solid phase by a change in ionic strength or pH, or addition of a substance that competes with the tag for binding to the receptor. For example, binding of metal chelate ligands immobilized on agarose and containing Ni.sup.2+ to a hexahistidine sequence is easily reversed by adding imidazole to the solution to compete for binding of the metal chelate ligand. Antibody-peptide binding can often be dissociated by raising the pH to 10.5 or higher.

Edwards discloses throughout the patent at e.g., col. 79, line 59 up to col. 80, line 40:

Microsequencing may be achieved by the established microsequencing method or by developments or derivatives thereof. Alternative methods include several solid-phase microsequencing techniques. The basic microsequencing protocol...[method] is conducted as a heterogeneous phase assay, in which the primer or the target molecule is immobilized or captured onto a solid support. To simplify the primer separation and the terminal nucleotide addition analysis, oligonucleotides are attached to solid supports or are modified in such ways that permit affinity separation as well as polymerase extension. The 5' ends and internal nucleotides of synthetic oligonucleotides can be modified in a number of different ways to permit different affinity separation approaches, e.g., biotinylation. If a single affinity group is used on the oligonucleotides, the oligonucleotides can be separated from the incorporated terminator regent. This eliminates the need of physical or size separation. More than one oligonucleotide can be separated from the terminator reagent and analyzed simultaneously if more than one affinity group is used. This permits the analysis of several nucleic acid species or more nucleic acid sequence information per extension reaction. The affinity group need not be on the priming oligonucleotide but could alternatively be present on the template. For example, immobilization can be carried out via an interaction between biotinylated DNA and streptavidin-**coated** microtitration wells or avidin-coated polystyrene particles. In the same manner, oligonucleotides or templates may be attached to a solid support in a high-density format….Other possible reporter-detection pairs include: ddNTP linked to dinitrophenyl (DNP) and anti-DNP alkaline phosphatase conjugate.. or biotinylated ddNTP and horseradish peroxidase-conjugated streptavidin with o-phenylenediamine as a substrate …….

Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use hapten such as biotin or dinitrophenol in the

method of anyone of Stahler et al as taught by Wu or Edwards or Gray. Each of Wu, Edwards and Gray teaches the conventionality of using various haptens that binds to different receptors such as nucleic acid or protein. One would have a reasonable expectation of success in using said hapten as successfully achieved by Edwards or Wu or Gray in purifying various compounds.

Response to Arguments

Applicant argues that Wu is directed to novel polynucleotides encoding MMP-29. Wu only discloses the attachment of his polynucleotides to haptens to facilitate purification. See page 127, lines 23-27, which indicates that the polypeptide is chemically modified with hapten groups in order to purify specific monoclonal antibodies by immunoprecipitation. Wu does not suggest or disclose the application of hapten groups to the carrier before, during or after the synthesis of receptors in situ.

In reply, while Wu does not disclose the application of hapten groups to the carrier before, during or after the synthesis of receptors in situ, each of the Stahler does. Stahler teaches that the carrier can be coated with e.g., peptides, (which would read on the claim hapten) or what will be the intended coating. Furthermore, Wu is employed not for the

purpose as argued but for its teachings that polynucleotide (receptor as broadly claim) can be attached to haptens albeit it is used to facilitate purification. The test for combining references is not what the individual references themselves suggest but rather what the combination of the disclosures taken as a whole would suggest to one of ordinary skill in the art. In re McLaughlin, 170 USPQ 209 CCPA 1971. The court must approach the issue of patentability in terms of what would have been obvious to one of ordinary skill in the art at the time the invention was made in view of the sum of all the relevant teachings in the art, not in view of the first one and then another of the isolated teachings in the art. In re Kuderna, 165 USPQ 575 CCPA 1970.

Applicant states that Gray discloses a method for the production of a multivalent polypeptide display library. Gray binds a biotin marked receptor to a solid phase coated with avidin to selectively remove the receptor from the solution. Thus Gray uses biotin for immobilizing antigens and antibodies.

Edwards discloses GSSP-2DNA and GSSP-2 polypeptides and the use of biotin as a capture molecule or a label. The hapten modified substrates are used for separating specific oligonucleotides. Applicant argues that neither Gray nor Edwards discloses the use of haptens in the synthesis of

receptors on a microfluidic carrier. Applicant contends that the newly cited references, Wu, Gray, and Edwards show only that haptens were well known in the art and can be used for separation or purifying receptors. None of the cited references suggest or disclose that haptens can be used in the synthesis of receptors and the quality and efficiency of the receptor synthesis can be easily determined or controlled due to the use of haptens. In the present invention, both the hapten group and the receptors are already immobilized on the microfluidic carrier before determining the analytes.

In response, please see the reply above under Wu since applicant merely presents the same arguments herein.

When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability. For the same reason, if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill. When considering obviousness of a combination of known elements, the operative question is thus "whether the improvement is more than the predictable use of prior art elements according to their established functions." KSR International Co. v. Teleflex Inc., 550 USPQ2d 1385 (2007).

No claim is allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

This application contains claims 20 and 21 drawn to non-elected inventions. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on (571) 272-0765. The fax phone number for the organization where this application or proceeding is assigned is 571 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/TERESA WESSENDORF/

Primary Examiner, Art Unit 1639